

45. The method of claim 44, wherein the random or partially random sequences comprise a length from about 5 nucleotides to about 10 nucleotides.

46. The method of claim 44, wherein the identifier tags are double-stranded sequences.

47. The method of claim 39, further comprising purifying a plurality of cypher-target nucleic acid complexes prior to sequencing, wherein the purified cypher-target nucleic acid complexes comprise nucleic acid molecules from specific genomic regions.

48. The method of claim 39, wherein prior to sequencing, the method further comprises amplifying each strand of the cypher-target nucleic acid complexes to produce a set of copies of original first strands of the cypher-target nucleic acid complexes and a set of copies of complementary original second strands of the cypher-target nucleic acid complexes.

49. The method of claim 39, wherein prior to comparing the first-strand sequencing reads with the second-strand sequencing reads, the method comprises grouping sequencing reads based on (i) the identifier tag sequences and (ii) sequence information from the double-stranded DNA molecules.

50. The method of claim 39, wherein each of the error-corrected sequences has only nucleotide bases at which the majority of first strand sequencing reads and second strand sequencing reads are in agreement.

51. The method of claim 50, wherein the method comprises calculating a mutation frequency among the plurality of double-stranded DNA molecules.

52. The method of claim 51, wherein the mutations are transition mutations.

53. The method of claim 50, wherein a sequence difference between the error-corrected sequence and the reference sequence is identified as a true mutation.

54. The method of claim 53, wherein the true mutation is a substitution or insertion mutation type.

55. The method of claim 53, wherein the true mutation is a transition mutation.

56. The method of claim 50, wherein the error-corrected sequences map to the reference sequence, and the method further comprises identifying a distribution of mutations in the double-stranded DNA molecules.

57. The method of claim 54, wherein the error-corrected sequences map to the reference sequence, and the method further comprises identifying a distribution of mutation types in the double-stranded DNA molecules.

58. The method of claim 39, wherein the error corrected sequence is generated by distinguishing erroneous nucleotides in one strand that lack a matched base change in the complementary strand, and wherein the erroneous nucleotides are the result of systematic or biological errors in one strand.

59. The method of claim 39, wherein the method comprises determining a genomic distribution of mutations with respect to the reference sequence.

60. A method of identifying effects of DNA damaging compounds, the method comprising:

- (a) providing a sample comprising a plurality of double-stranded DNA molecules from a patient that has been treated with a compound;
- (b) preparing a sequencing library from the sample by ligating cypher polynucleotides to the double-stranded DNA molecules to form double-stranded cypher-target nucleic acid complexes, wherein the cypher polynucleotides comprise identifier tags selected from a plurality of distinct identifier tag sequences;
- (c) for each cypher-target nucleic acid complex among a plurality of the cypher-target nucleic acid complexes, generating a set of copies of a first strand of the cypher-target nucleic acid complex and a set of distinct yet related copies of a complementary second strand of the cypher-target nucleic acid complex;
- (d) sequencing one or more copies of the first and complementary second strands to produce a plurality of first-strand sequencing reads and a plurality of distinct yet related second-strand sequencing reads;
- (e) for each cypher-target nucleic acid complex among a plurality of the cypher-target nucleic acid complexes, comparing the first-strand sequencing reads with the second-strand sequencing reads to identify nucleotides in the first strand that have a corresponding complementary nucleotide in the second strand;
- (f) comparing an error-corrected sequence generated from the first strand sequencing reads and second strand sequencing reads to a reference sequence to determine one or more of a mutation, a genomic distribution of mutations, a mutation frequency, sequence heterogeneity, or DNA damage; and
- (g) based on the comparing step, identifying DNA damage from the compound.

61. The method of claim 60, wherein the error corrected sequence is generated by distinguishing erroneous nucleotides in one strand that lack a matched base change in the complementary strand, and wherein the erroneous nucleotides are the result of systematic or biological errors in one strand.

62. The method of claim 60, wherein step (a) further comprises providing a plurality of samples from a plurality of patients treated with the compound.

63. The method of claim 60, further comprising purifying a plurality of cypher-target nucleic acid complexes prior to sequencing, wherein the purified cypher-target nucleic acid complexes comprise nucleic acid molecules from specific genomic regions, and wherein the specific genomic regions comprise mutations common to most cells of a tumor.

64. The method of claim 60, wherein the double-stranded DNA molecules comprise a deaminated cytosine.

65. The method of claim 64, wherein the method further comprises enzymatically treating the double-stranded DNA molecules to repair damaged ends thereof prior to the ligating.

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